

REMARKS

The Final Office Action mailed March 3, 2009, has been carefully studied. The claims in the application are amended above to essentially rewrite claim 4 in independent form by incorporating the dependent part of claim 4 into claim 2, by amending claim 5 to make it dependent from claim 2, and by canceling redundant claims 8 and 9.

Applicants believe and respectfully maintain that their claims define patentable subject matter and therefore should be allowed. Favorable reconsideration and allowance are therefore earnestly solicited.

Acknowledgement by the PTO of the receipt of Applicants' papers filed under §119 is noted.

Claims 2-5 have been rejected under the first paragraph of §112 on the basis purported failure to comply with the written description requirement with respect to the feature that the heat treatment is sufficient to inactivate virus. This rejection is respectfully traversed.

The added terminology criticized in the rejection is absolutely clear from Applicants' specification, and therefore fully complies with the description requirement and does not constitute prohibited new matter. Indeed, the subject matter in question appears repeatedly in Applicants' specification, noting for example the following text appearing in the exact English translation of Applicants' specification as filed:

1. See the text at page 2, lines 19-22 relating to the indispensability of inactivating viruses. Also see page 3, line 1. In lines 6-9 of page 3, it is pointed out that "each... individual approach [in the prior art] alone would not likely provide complete inactivation or complete removal of viruses"; the clear implication then is that the present invention is intended to depart from the prior art by providing complete inactivation or complete removal of viruses. More of the same appears in the bottom paragraph on page three. The text at page 6, e.g., lines 14-18, makes explicit that an object of the invention is "to solve the problems as described above."

2. In the paragraph spanning pages 6 and 7, and in particular at page 7, lines 3-6, it is stated explicitly that the method involves "a heat treatment in a liquid state... **for inactivation of viruses...**" (emphasis added)

3. At page 10, lines 9-16, and particularly at lines 14-16, it is stated as follows: "By performing a step of filtration of the present invention **before a heat treatment for inactivation of viruses,...** a good filtration property may be obtained." (emphasis added)

It is therefore absolutely clear that the added language "sufficient to inactivate virus" is fully supported and described as part of Applicants' invention as per the first paragraph of §112 and does not constitute prohibited new matter. Even if the added language were only implicit, it would meet the requirements of the first paragraph of §112, as this would at most be an issue of *ipsis verbis*. Please see, for example, MPEP 2163:

While there is no *in haec verba* requirement, newly added claim limitations must be supported

by the specification through express, implicit,
or inherent disclosure.

And:

The examiner has the initial burden...of presenting evidence or reasons why a person skilled in the art would not recognize that the written description...provides support for the claims.
There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed,... [citation omitted; emphasis added]

And:

The examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims. [citation omitted]

And:

An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. [citation omitted]

And MPEP 2163.02:

The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement.

It should be absolutely clear from Applicants' specification that Applicants' claims, as previously amended, fully meet all the requirements of 35 USC §112, first paragraph. Withdrawal of the rejection is in order and is respectfully requested.

Claims 2, 4 and 6 are again rejected as obvious under §103 from Winge in view of Chang. This rejection is respectfully traversed for the reasons of record, respectfully repeated by reference, and for the additional reasons set forth below.

The gist of the process for preparing an albumin preparation according to the present invention lies in that it comprises (a) the step of treating an albumin-containing solution with an anion exchanger and/or a prefilter, (b) the step of filtration with a virus-removing membrane, and (c) the step of heat treatment in a liquid state, with the steps (a) to (c) being performed in this exact order. None of the cited prior art references teach the order of the steps of the claimed process to the person of ordinary skill in the art so that the steps (a) to (c) above are or are to be performed in this exact order.

Filtration with a virus-removing membrane, which has been used for removal of pathogens such as viruses in a chemical solution, has not hitherto been applied to a production process of an albumin preparation in a commercial scale production, or indeed any production described in the art. Under the circumstances, the present inventors have found a good filtration property to complete the present invention (cf. page 6, lines 6-13).

In application of filtration with a virus-removing membrane, which has been used for removal of pathogens such as viruses in a chemical solution, to a production process of an albumin preparation in a commercial actual scale of production not attempted hitherto, the present inventors have found a good filtration property to complete the present invention.

In accordance with the present invention, an albumin-containing solution, before any heat treatment, was found to exhibit a good

filtration property in filtration with a virus-removing membrane. Besides, it was confirmed that pretreatment with an anion exchanger and/or prefiltration surprisingly provides that a volume of filtration per area of a filter increases without manipulating chemical conditions of the solution (cf. page 7, lines 8-16).

In filtration with a virus-removing membrane in accordance with the present invention, an albumin-containing solution before a heat treatment was found to exhibit a good filtration property.

Besides, it was confirmed that pretreatment with an anion exchanger and/or prefiltration in a preferable embodiment may provide for an effect that a volume of filtration per area of a filter increases without manipulating chemical conditions of the solution.

The U.S. patent law is clear that what an applicant states in his or her specification is to be accepted by the PTO in the absence of evidence or good reasoning to the contrary, and there is no evidence or good reasoning contrary to what is stated in Applicants' specification regarding the claimed invention.

Winge merely discloses the possible applicability of a method of virus-filtration with a virus-removing membrane to a solution of various proteins. Chang also merely discloses a method of purifying albumin (no mention is made of the presence of virus) using a combination of a precipitating process and an anion exchange chromatography. However, neither Winge nor Chang teach the process for preparing an albumin preparation which comprises (a) the step of treating an albumin-containing solution with anion exchanger and/or a prefilter, (b) the step of filtration with a virus-removing membrane, and (c) the step of heat treatment in a liquid state, wherein the steps (a) to (c) are performed in this exact order.

Since the prior art references do not teach the importance of the order of each of the steps (a) to (c), even if one of ordinary skill in the art were motivated to modify the method of Winge by using a combination of purification steps including heat treatment or anion exchange filtration as taught by Chang, the presence of such motivation being respectfully denied for the reasons of record, the claimed process as amended could still not have been attained. A consideration of the references together does not and would not have led the person of ordinary skill in the art to the claimed subject matter, and therefore no *prima facie* case of obviousness exists.

Moreover, there is no way that a person of ordinary skill in the art would have any reasonable expectation of the success achieved by Applicants. The references do not even hint at the possibility of obtaining Applicants' achievements.

With regard to the rejection of claim 6, again it is noted that Winge merely discloses the possible applicability of a method of virus-filtration with a virus-removing membrane to a solution of various proteins, and Chang merely discloses a method of purifying albumin using a combination of a precipitating process and an anion exchange chromatography, but neither Winge nor Chang teach the process as claimed in claim 6. Specifically, claim 6 is drawn to a process for pretreating an albumin-containing solution before a step of filtration with a virus-removing membrane which comprises (a) the step of treating said albumin-containing solution with an anion exchanger and/or a prefilter and (b) the step of filtration of said albumin-containing solution with a virus-removing membrane wherein the steps (a) to (b) are performed in this exact order, which process is taught neither in Winge nor in Chang.

No possible combination, even if the references were to be considered together, would lead the skilled worker to the claimed, required order of steps.

Withdrawal of the rejection is in order and is respectfully requested.

Claims 2, 3, 5 and 7-9 have been rejected under §103 as obvious from Winge in view of Chang and further (as understood) in view of Burnouf (reference AH of the IDS filed January 6, 2006). This rejection is respectfully traversed insofar as it is understood.

Applicants do not understand the reference in the statement of the rejection to a website, and therefore Applicants do not fully understand what the Examiner is relying on. Is this intended to be a fourth reference in combination with the other three?

Regardless, insofar as claims 2, 3 and 5 are concerned, Applicants note that claim 4 is not included in this rejection. As claims 2, 3 and 5 all incorporate the subject matter of previous claim 4, Applicants understand that they need not address this rejection as regards claims 2, 3 and 5.

Claims 8 and 9 have been deleted and therefore present rejection need not be addressed as regards claims 8 and 9 at the present time.

With respect to claims 7-9, Applicants note that claim 7 depends from and incorporates the subject matter of claim 6. The additional prior art applied against claims 7-9 in comparison with claim 6 has not been cited to overcome the deficiencies of the

rejection as applied to claim 6, and therefore claims 7-9 define nonobvious subject matter for the same reasons as claim 6, as pointed out above.

Withdrawal of the rejection is in order and is respectfully requested.

In addition to Applicants' rebuttal of the rejections as set forth above, coupled with what has been set forth in the Reply of December 11, 2008, respectfully repeated by reference, Applicants wish to briefly address some of the points raised in the part of the final rejection commencing at about the middle of page 12 under the heading "Response to Arguments".

The Examiner says that Applicants' statement that "the heat-shock treatment of example 9 of Chang is not intended to inactivate virus", is "not substantiated by the Applicant." Respectfully, the burden is on the Examiner to establish a case of *prima facie* obviousness based on what the references disclose. Chang speaks for itself, and it does not disclose that the heat-shock treatment of example 9 is intended to inactivate virus. This unsupported conclusion comes from the Examiner, not the reference which says nothing about any virus. Also, there can be no inherency because there is no virus in Chang.

As regards Applicants' previously stated (and still maintained) position that "there is no reason" to combine the references, the mere fact that the references are in the same field, or even that they seek the same objective, does not provide a reason for their combination. Applicants again note that Chang does not even indicate the presence of virus. Moreover, Chang

teaches away from the example 9 method, and therefore the person of ordinary skill in the art would never adopt (relying on Chang) what Chang teaches is undesirable.

Respectfully, the PTO has not answered or rebutted this fact.

As regard the Examiner's reliance on *KSR*, it is respectfully noted that *KSR* supports Applicants' position. As previously pointed out, Chang teaches away from the prior acetone and heat-shock purification method, and it cannot have been obvious to adopt something from Chang which Chang effectively denigrated. It would not have been "obvious to try" something which the prior art teaches against.

See, for example, *Takeda v. AlphaPharm* 83 USPQ2d 1169, 1174 (Fed. Cir. 2007). The court stated that the Supreme Court, in *KSR*, "acknowledged the importance of identifying 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination." And that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." The Federal Circuit rejected "obvious to try" (page 1176) because there was no good reason to try, as is the situation in the present case.

Also see *Eisai v. Dr. Reddy's Laboratories*, 87 USPQ2d 1452, 1456, 1457 (Fed. Cir. 2008). Here the Federal Circuit affirmed the decision of the lower court ruling that the parties challenging validity of the patent failed to prove a *prima facie* case of obviousness because they did not provide an adequate explanation as to why a person of ordinary skill in the art would

have been motivated to make the change leading to the claimed invention.

The PTO position in the present application appears to be that practically anything is "obvious to try", which makes everything unpatentable. There has to be a viable reason, and when one reference teaches away from a particular operation, it cannot be reasonably said that it would be obvious to adopt such a criticized expedient, or even obvious to try such a criticized expedient.

The Supreme Court itself stated in *KSR* as follows:

[W]hen the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious. [*KSR*, 550 U.S. at 416 (citing *Adams*, 383 U.S. at 51-52)].

It has been pointed out above and earlier that Chang denigrates that for which it is relied upon. Chang thus **teaches away from** the present invention, and this cannot be reasonably denied.

Since *KSR*, not only has the Federal Circuit held many claims to be patentable and valid, but so has the PTO Board of Patent Appeals and Interferences. Among these are *Ex parte Wada et al.*, Appeal 2007-3733 (2008); *Ex parte McDonald*, Appeal 2009-002329 (2009); *Ex parte Smith*, Appeal 2008-003903 (2009); *Ex parte Van der Winkle et al.*, Appeal 2009-0843 (2009). There are many, many others. In all these cases, the examiner was reversed, and *KSR* was cited. The PTO cannot validly rely on *KSR* to reject everything, and a reference teaching away from what an applicant does (as Chang does in the present case) is strong evidence of non-obviousness.

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Again, the prior art rejection is unjustified and should be withdrawn. Such is respectfully requested, as are favorable reconsideration and allowance.

Respectfully submitted,

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